

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:

Claim 1 (currently amended). A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

Z is selected from:

HO_2C ;

$\text{HO}(\text{H})\text{N}(\text{O})\text{C}$;

$\text{H}(\text{O})\text{C}-\text{N}(\text{OH})$;

$\text{CH}_3(\text{O})\text{C}-\text{N}(\text{OH})$;

$\text{CH}_3(\text{H})\text{N}(\text{O})\text{C}-\text{N}(\text{OH})$;

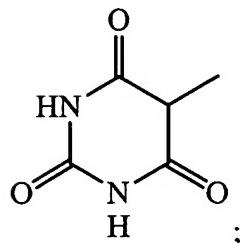
HS ;

$\text{H}_2\text{N}(\text{O})_2\text{S}$;

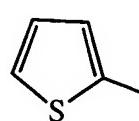
$\text{CH}_3(\text{H})\text{N}(\text{O})_2\text{S}$;

$\text{HO}(\text{O})\text{P}$;

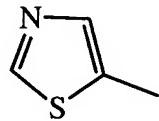
$(\text{HO})_2(\text{O})\text{P}$;



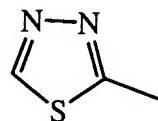
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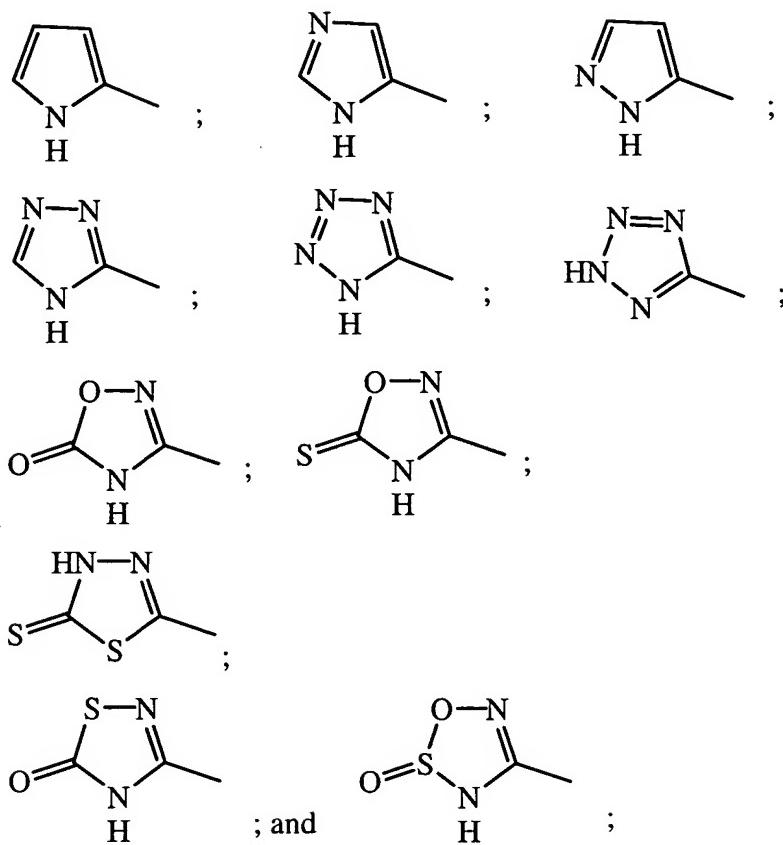
;



;



;



L is selected from:

C_3 - C_5 alkylene;

Substituted C_3 - C_5 alkylene;

3- to 5-membered heteroalkylene; and

Substituted 3- to 5-membered heteroalkylene;

Substituted L groups contain 1 or 2 substituents on a carbon atom or nitrogen atom independently selected from:

HO ;

CN ; and

CF_3 ;

wherein each substituent on a carbon atom may further be independently F, and wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group $C=O$;

R^1 is independently selected from:

C₅ or C₆ cycloalkylenyl-(C₁-C₈ alkylenyl);
Substituted C₅ or C₆ cycloalkylenyl-(C₁-C₈ alkylenyl);
5- or 6-membered heterocycloalkylenyl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heterocycloalkylenyl-(C₁-C₈ alkylenyl);
Phenyl-(C₁-C₈ alkylenyl);
Substituted phenyl-(C₁-C₈ alkylenyl);
5- or 6-membered heteroarylenyl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heteroarylenyl-(C₁-C₈ alkylenyl);
Phenyl;
Substituted phenyl;
Naphthyl;
Substituted naphthyl;
5- or 6-membered heteroaryl;
Substituted 5- or 6-membered heteroaryl;
8- to 10-membered heterobiaryl; and
Substituted 8- to 10-membered heterobiaryl;

R² is independently selected from:

H;
C₁-C₆ alkyl;
Phenyl-(C₁-C₈ alkylenyl);
Substituted phenyl-(C₁-C₈ alkylenyl);
Naphthyl-(C₁-C₈ alkylenyl);
Substituted naphthyl-(C₁-C₈ alkylenyl);
5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
Phenyl-O-(C₁-C₈ alkylenyl);
Substituted phenyl-O-(C₁-C₈ alkylenyl);
Phenyl-S-(C₁-C₈ alkylenyl);

Substituted phenyl-S-(C₁-C₈ alkylenyl);
Phenyl-S(O)-(C₁-C₈ alkylenyl);
Substituted phenyl-S(O)-(C₁-C₈ alkylenyl);
Phenyl-S(O)₂-(C₁-C₈ alkylenyl); and
Substituted phenyl-S(O)₂-(C₁-C₈ alkylenyl);

Each substituted R¹ group contains from 1 to 3 substituents, and each substituted R² group contains from 1 to 4 substituents, wherein each substituent is independently on a carbon or nitrogen atom, independently selected from:

C₁-C₆ alkyl;
CN;
CF₃;
HO;
(C₁-C₆ alkyl)-O;
(C₁-C₆ alkyl)-S(O)₂;
H₂N;
(C₁-C₆ alkyl)-N(H);
(C₁-C₆ alkyl)₂-N;
(C₁-C₆ alkyl)-C(O)O-(C₁-C₈ alkylenyl)_m;
(C₁-C₆ alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)_m;
(C₁-C₆ alkyl)-C(O)N(H)-(C₁-C₈ alkylenyl)_m;
(C₁-C₆ alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)_m;
H₂NS(O)₂-(C₁-C₈ alkylenyl);
(C₁-C₆ alkyl)-N(H)S(O)₂-(C₁-C₈ alkylenyl)_m;
(C₁-C₆ alkyl)₂-NS(O)₂-(C₁-C₈ alkylenyl)_m;
3- to 6-membered heterocycloalkyl-(G)_m;
Substituted 3- to 6-membered heterocycloalkyl-(G)_m;
5- or 6-membered heteroaryl-(G)_m;
Substituted 5- or 6-membered heteroaryl-(G)_m;
(C₁-C₆ alkyl)-S(O)₂-N(H)-C(O)-(C₁-C₈ alkylenyl)_m; and
(C₁-C₆ alkyl)-C(O)-N(H)-S(O)₂-(C₁-C₈ alkylenyl)_m;

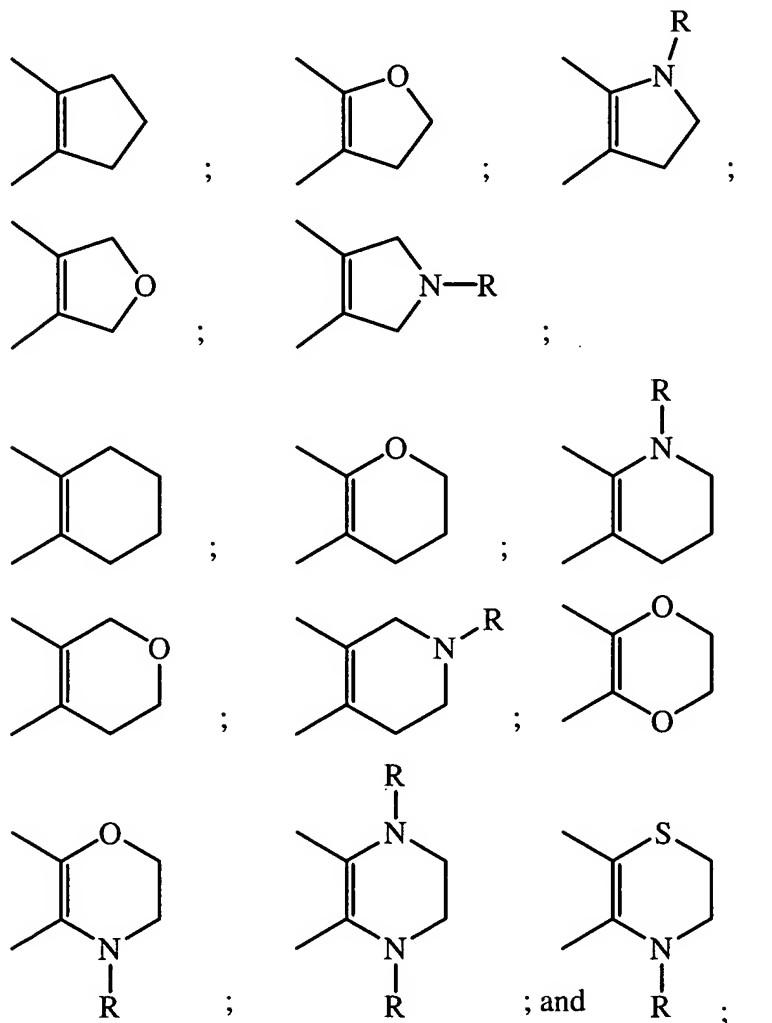
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO_2C ;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group $\text{C}=\text{O}$;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



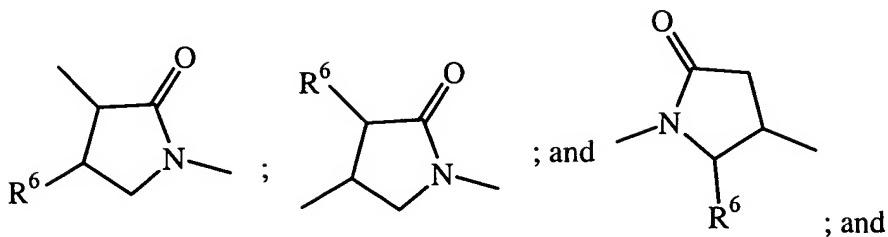
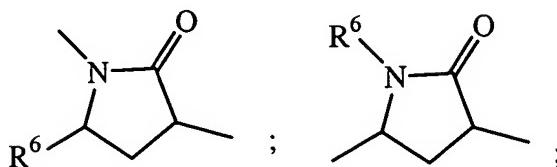
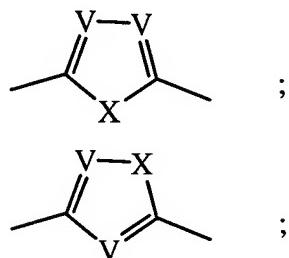
R is H or $\text{C}_1\text{-}\text{C}_6$ alkyl;

G is CH_2 ; O, S, S(O) ; or S(O)_2 ;

Each m is an integer of 0 or 1;

Q, when bonded to a nitrogen atom in group D, is selected from:

- OC(O);
- CH(R⁶)C(O);
- OC(NR⁶);
- CH(R⁶)C(NR⁶);
- N(R⁶)C(O);
- N(R⁶)C(S);
- N(R⁶)C(NR⁶);
- SC(O);
- CH(R⁶)C(S);
- SC(NR⁶);
- C≡CCH₂;



Q, when bonded to a carbon atom in group D, is as defined above and may further be selected from:

- OCH₂;
- N(R⁶)CH₂;
- trans-(H)C=C(H);

cis-(H)C=C(H);

C≡C;

CH₂C≡C;

CF₂C≡C;

C≡CCF₂;

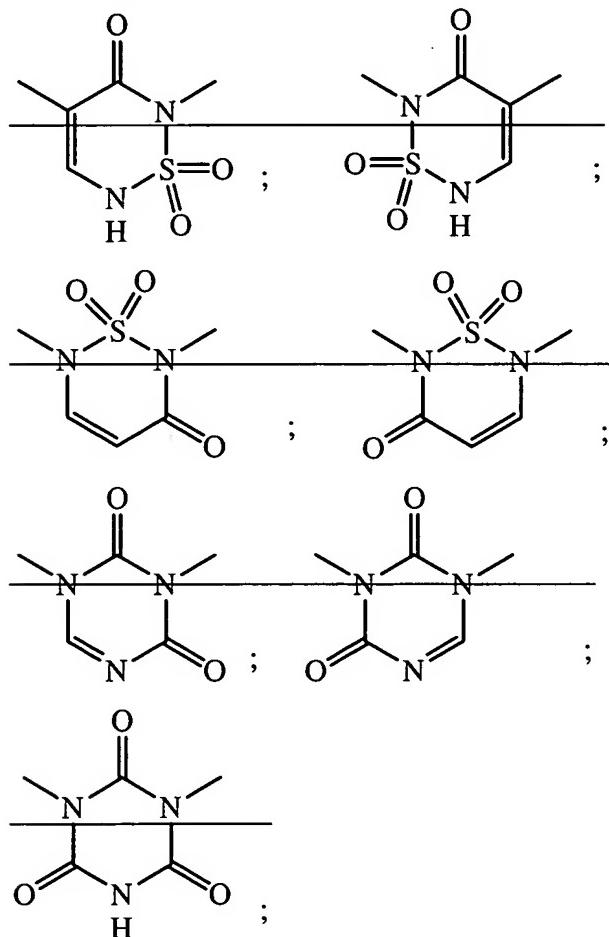
Each R⁶ independently is H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl; 3- to 6-membered

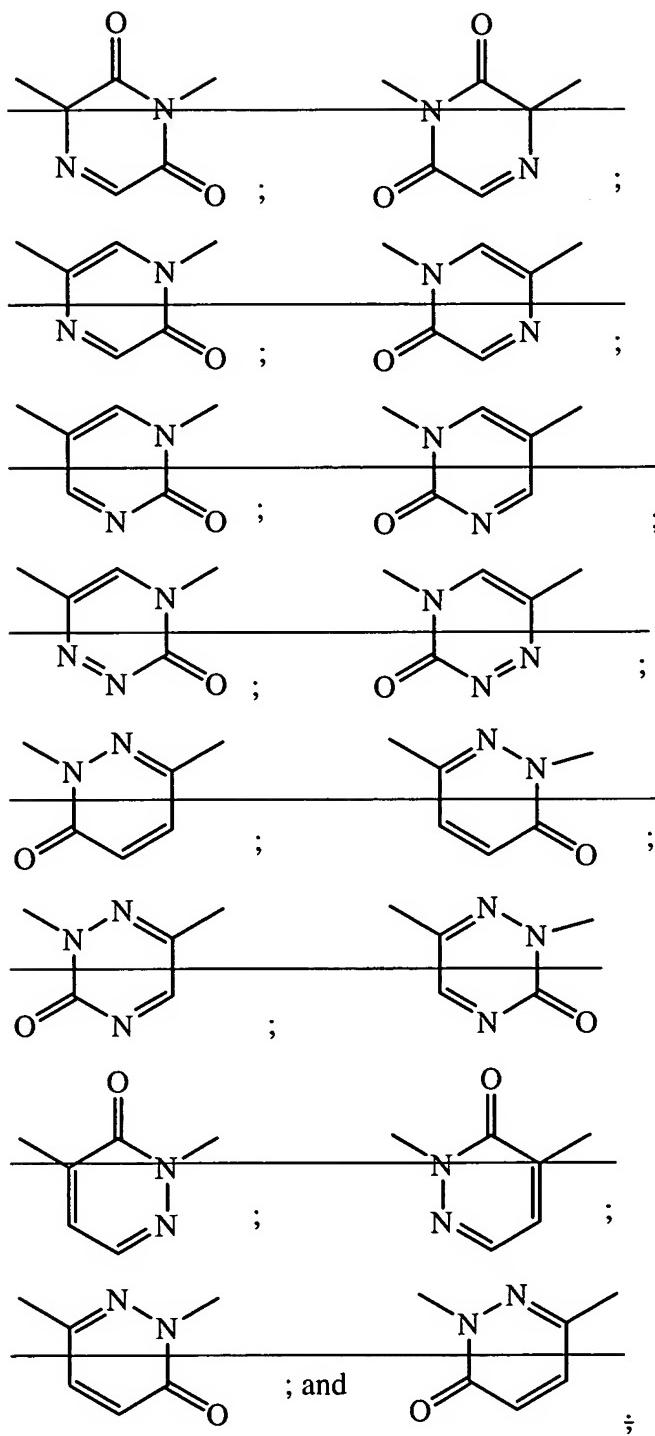
heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

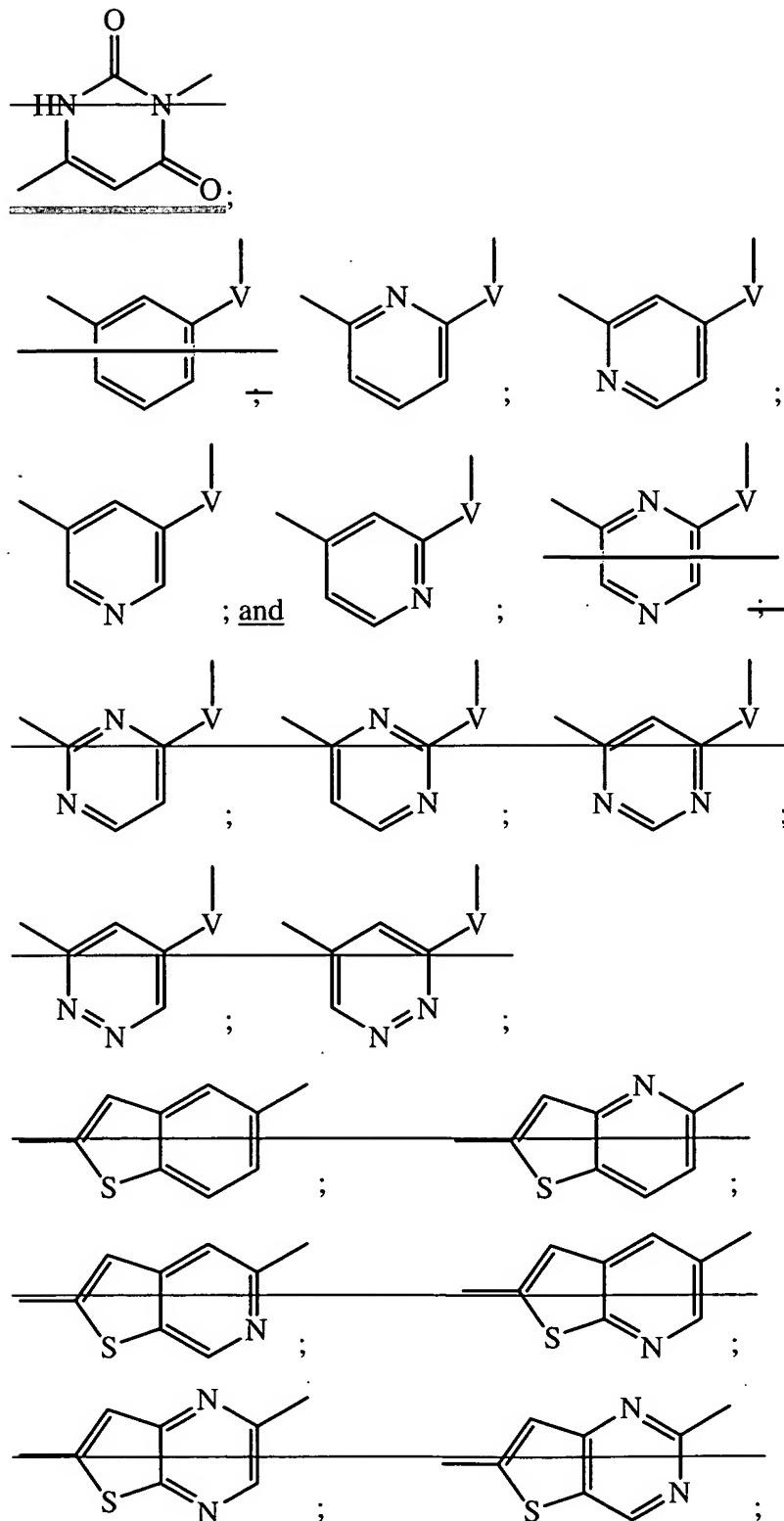
X is O, S, N(H), or N(C₁-C₆ alkyl);

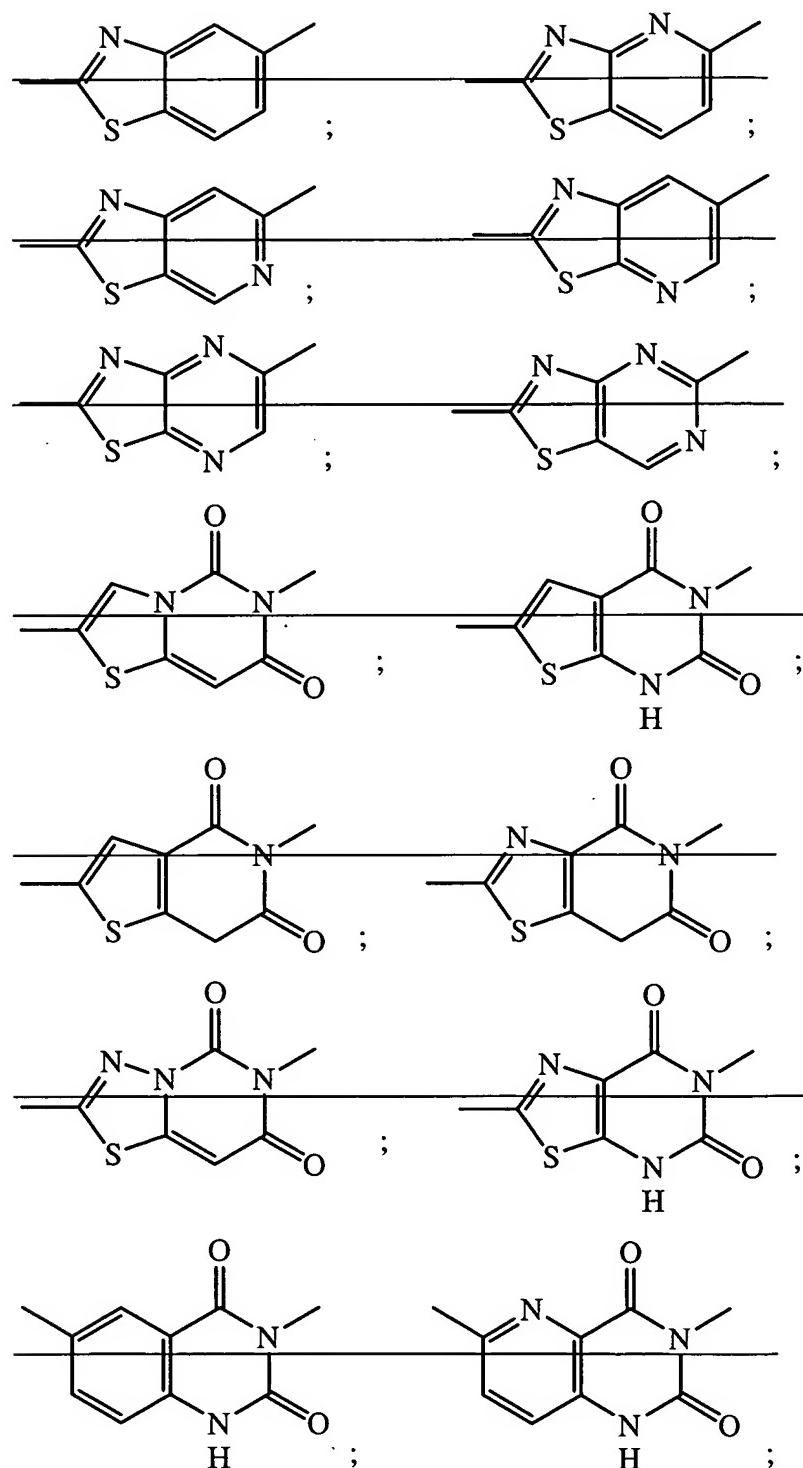
Each V is independently C(H) or N;

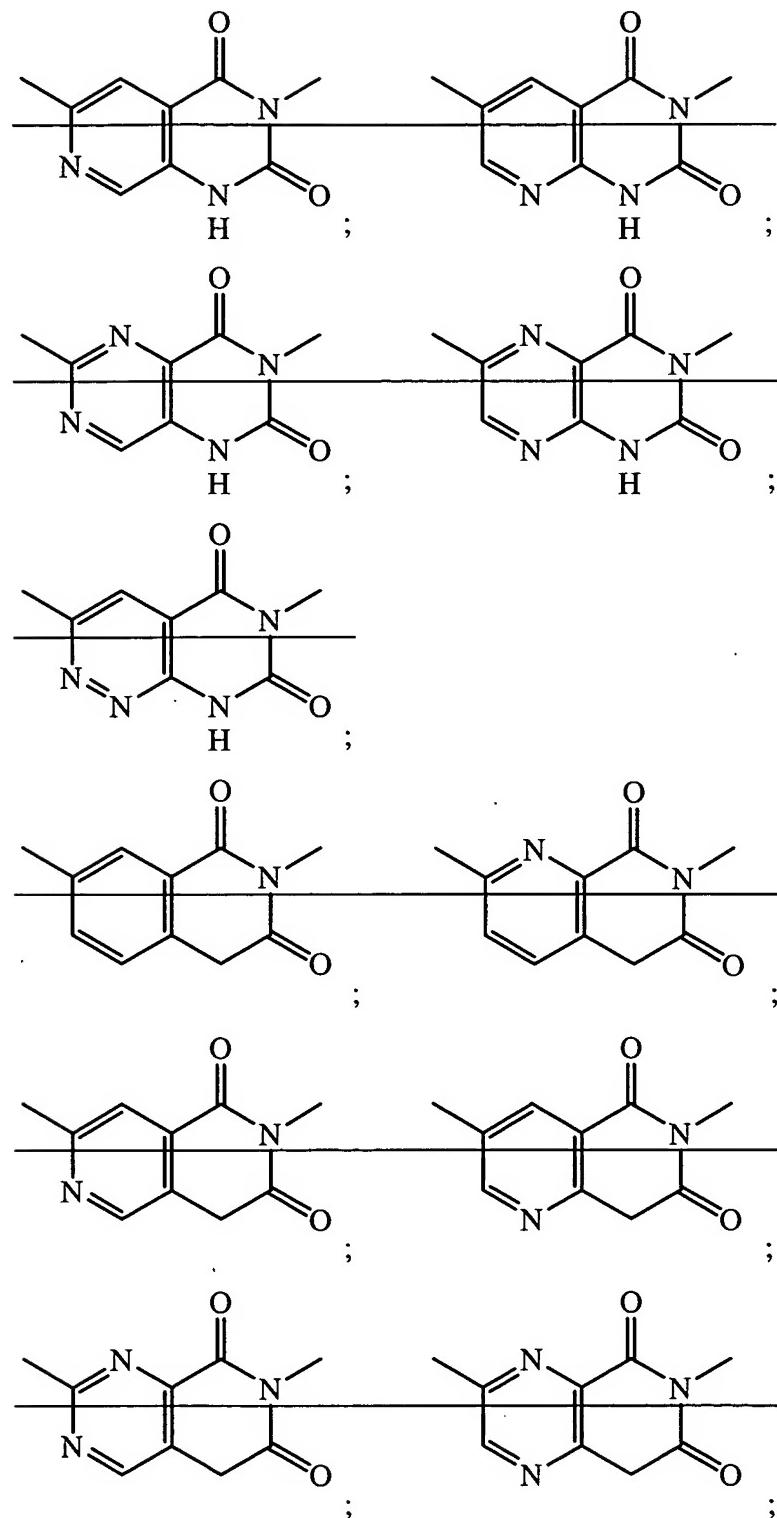
D is a cyclic diradical group selected from:

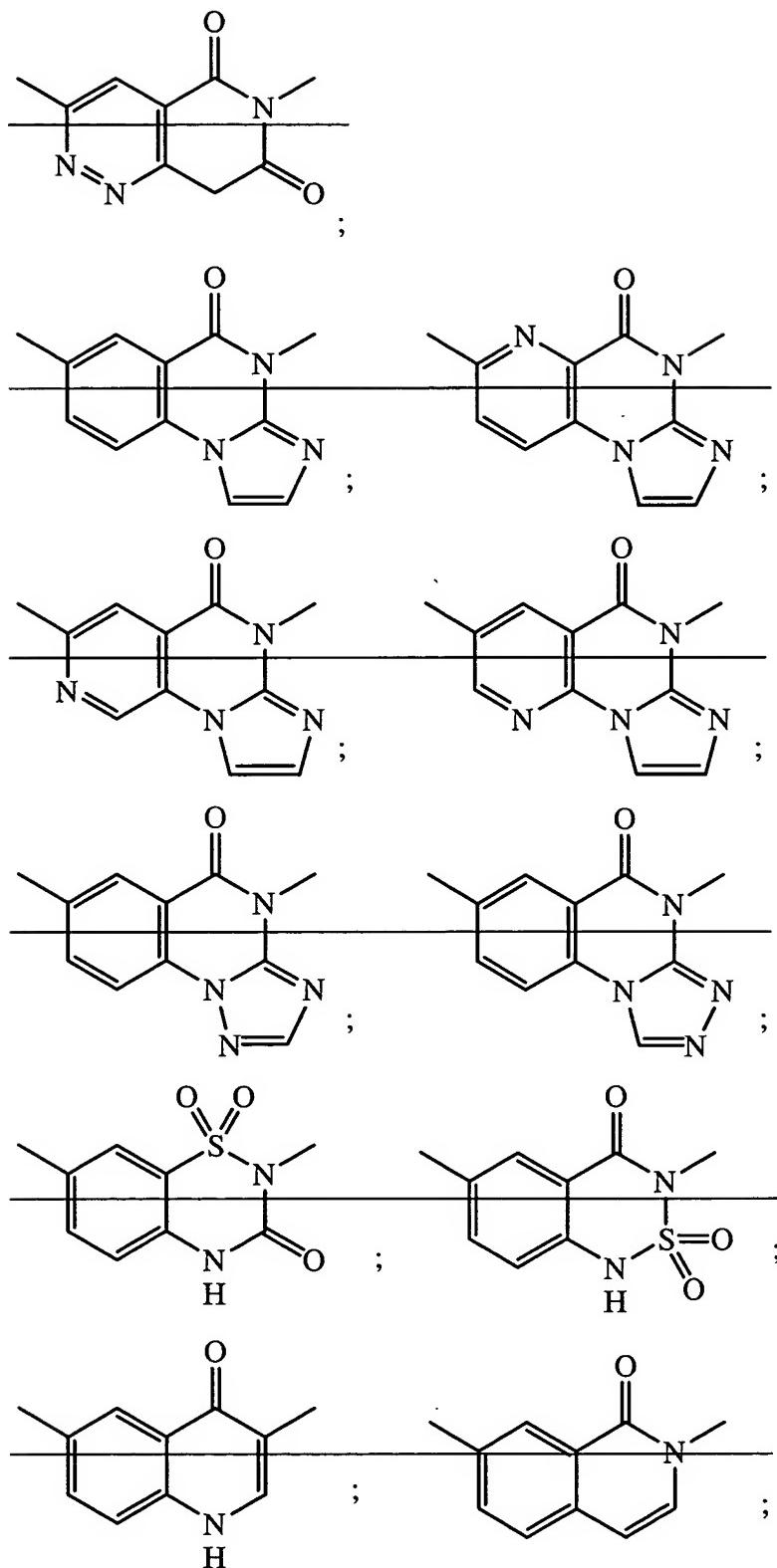


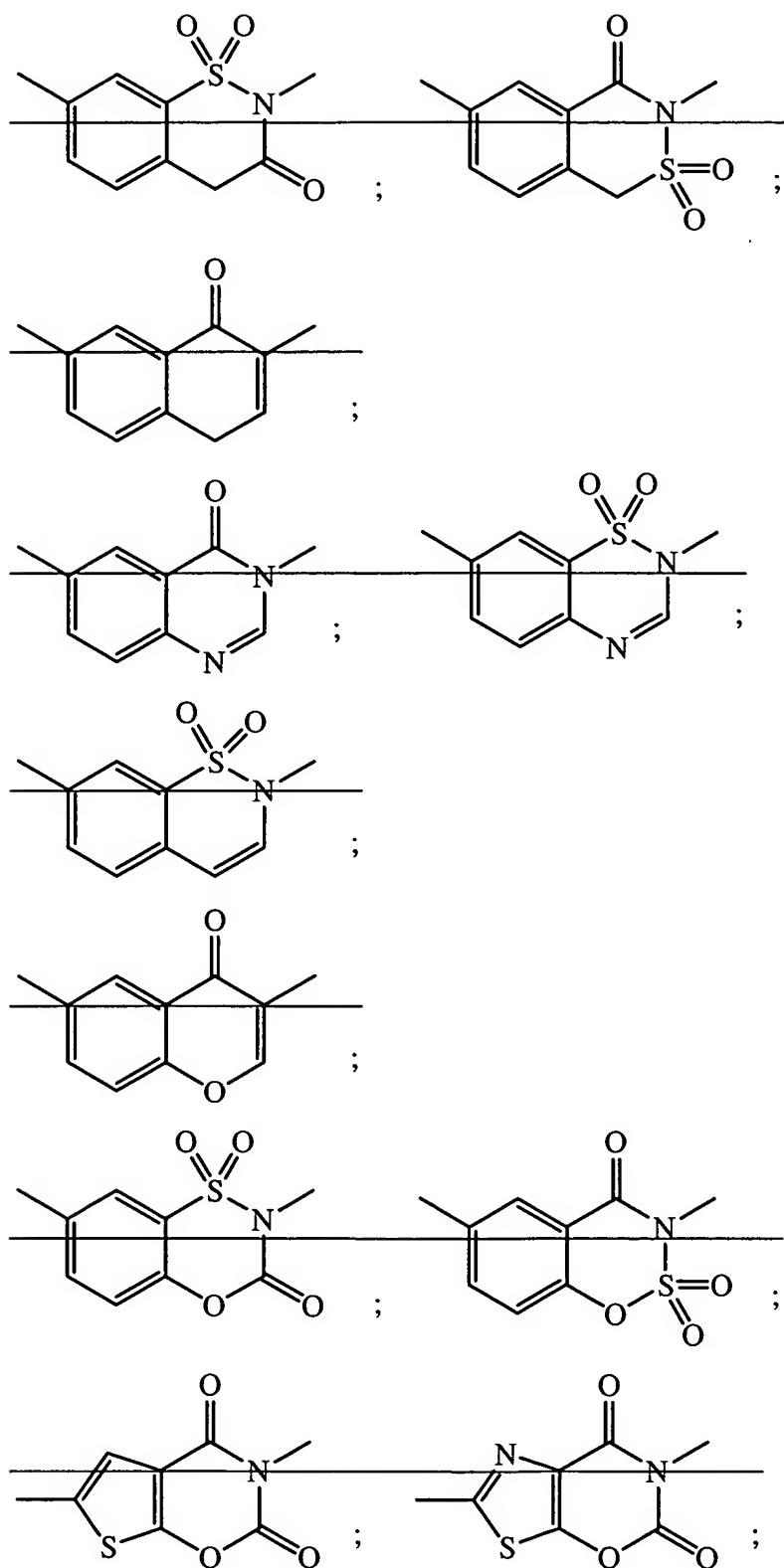


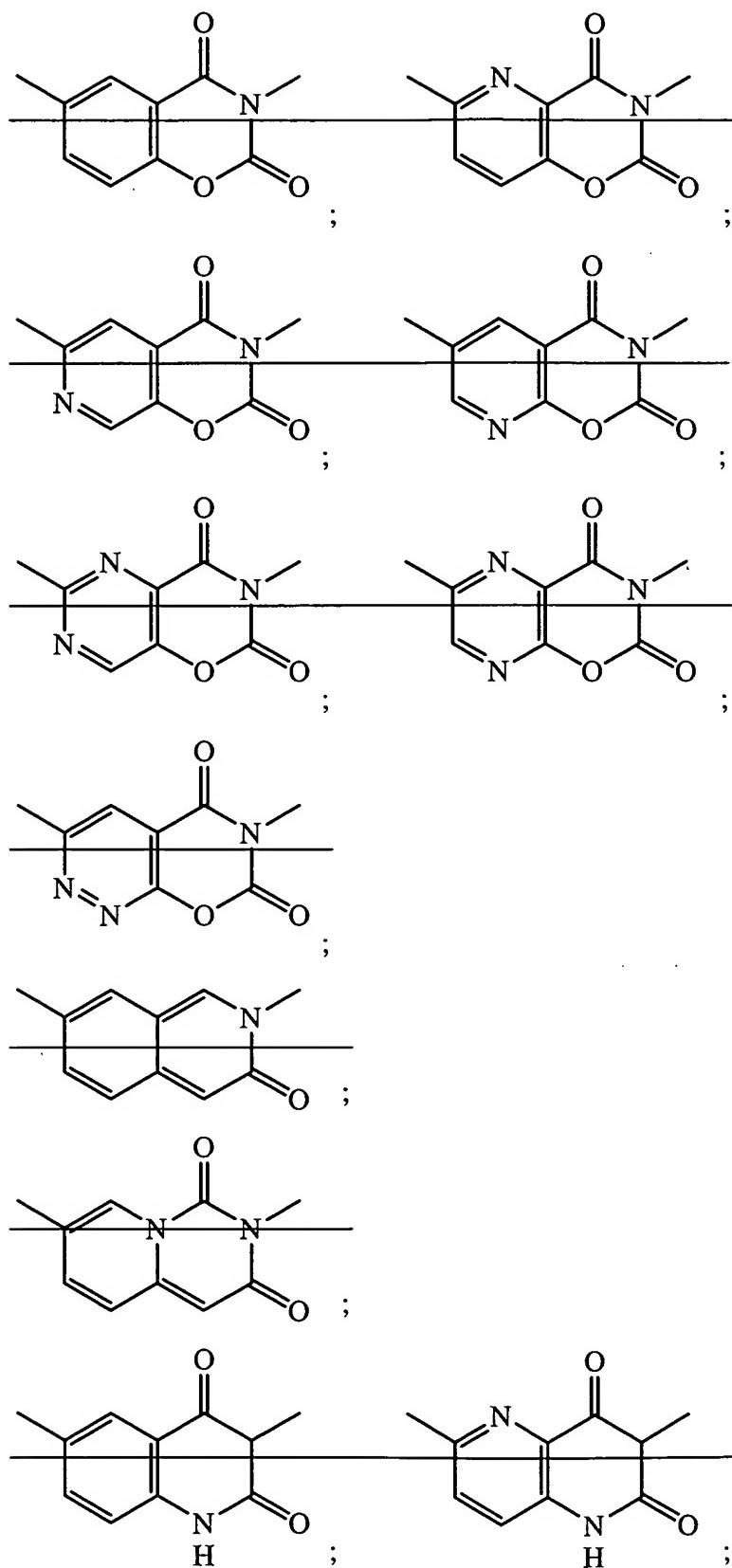


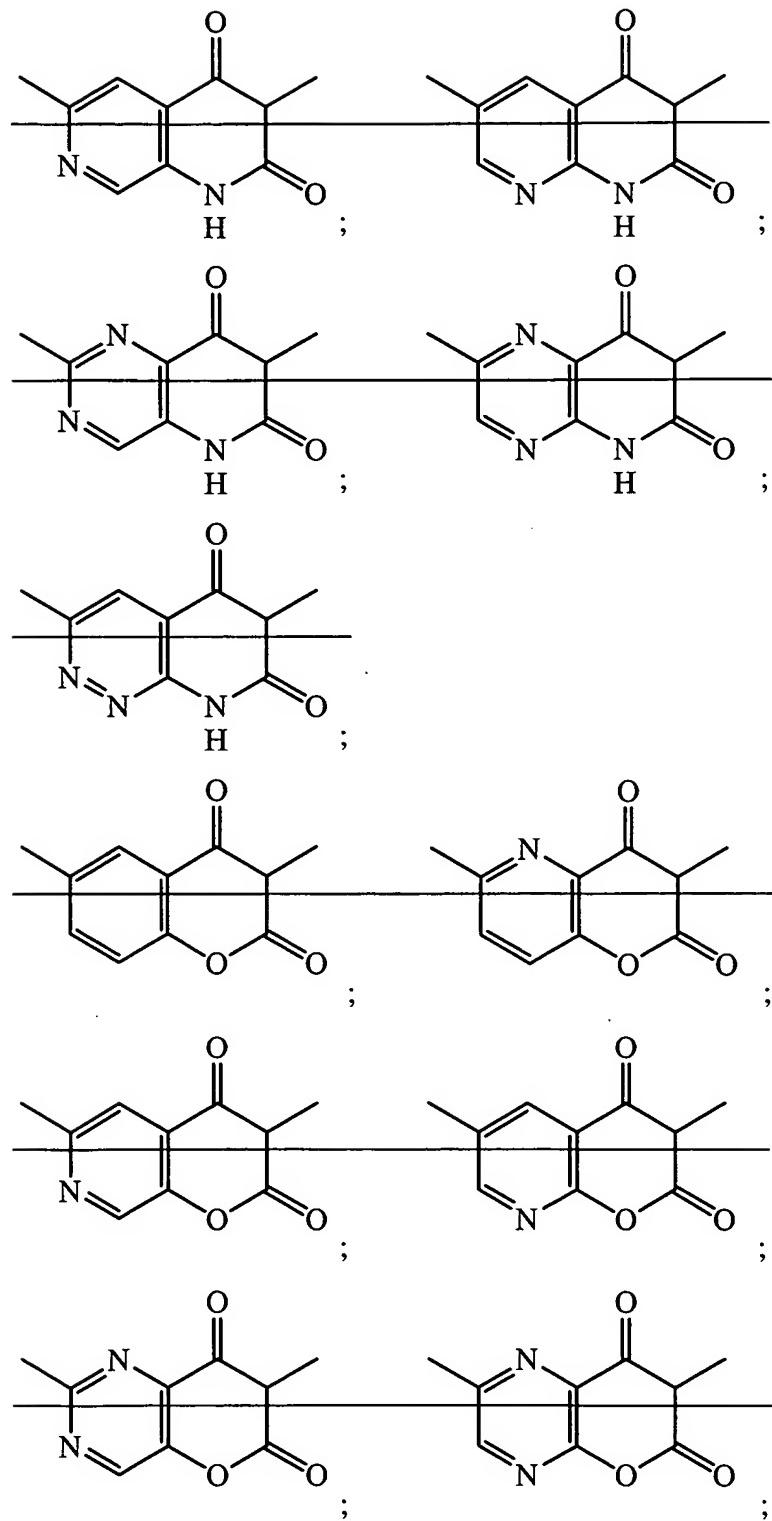


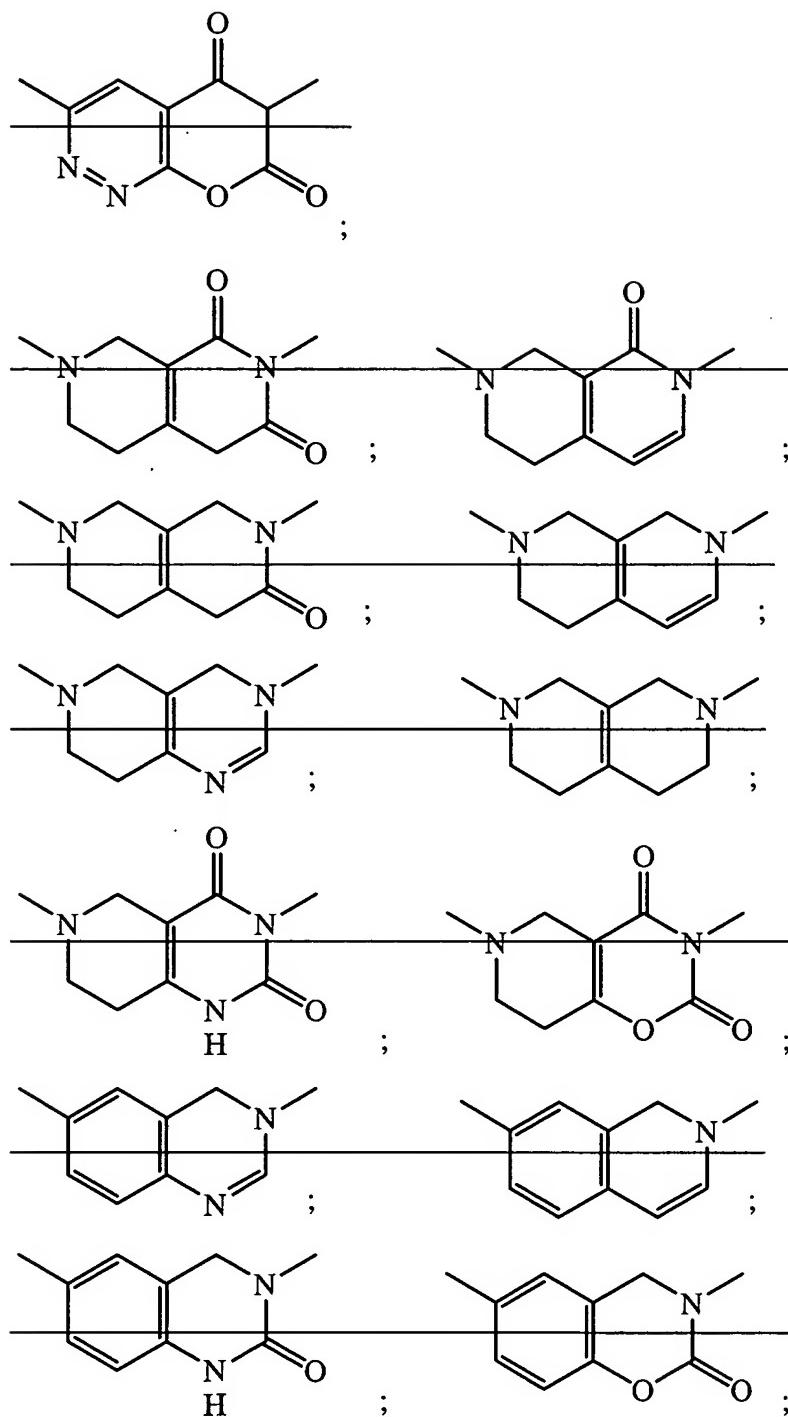


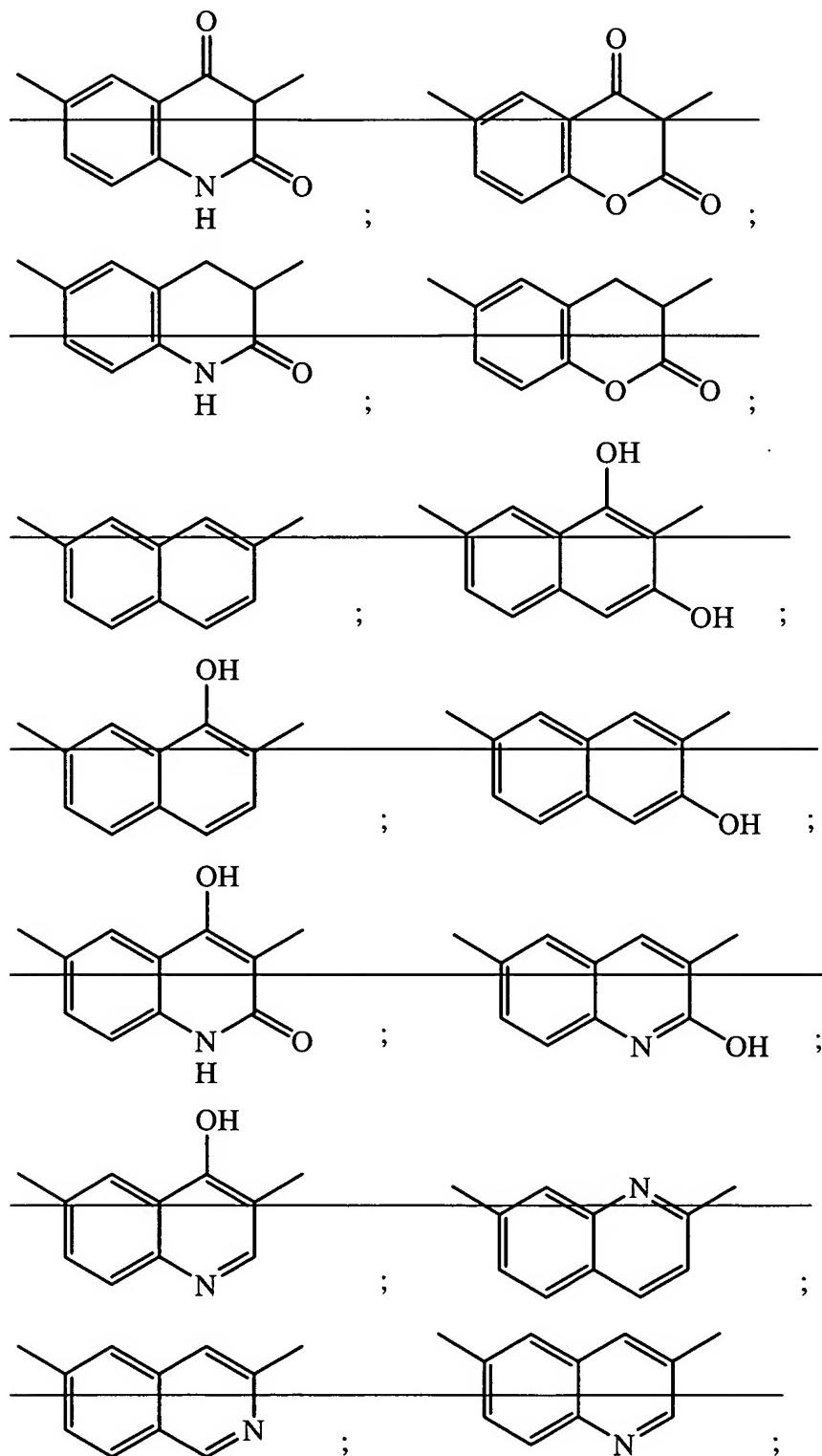


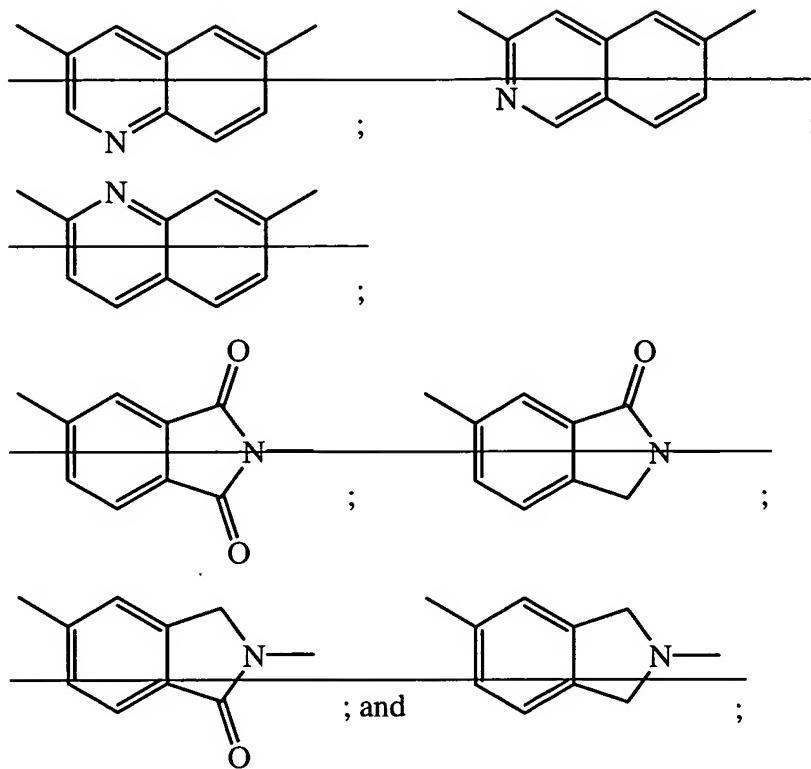












wherein the group D may be unsubstituted or substituted on a carbon atom or a nitrogen atom by replacement of a hydrogen atom with a group selected from:

CH_3 ;

CF_3 ;

C(O)H ;

CN ;

HO ;

CH_3O ;

$\text{C(F)H}_2\text{O}$;

$\text{C(H)F}_2\text{O}$; and

CF_3O ;

wherein a carbon atom in the group D may further be substituted with F;

V^1 is a 5-membered heteroarylenyl containing carbon atoms and from 1 to 4

heteroatoms selected from 1 O, 1 S, 1 NH, 1 N($\text{C}_1\text{-C}_6$ alkyl), and 4 N,

wherein the O and S atoms are not both present, and wherein the

heteroarylenyl may optionally be unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

wherein each C₈-C₁₀ bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

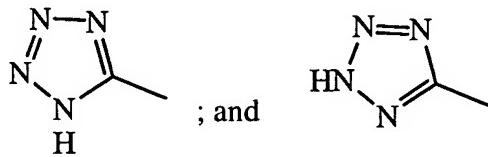
wherein each heterocycloalkylenyl is a ring diradical that contains carbon atoms and from 1 to 3 heteroatoms independently selected from 1 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 2 N(H), and 2 N(C₁-C₆ alkyl), and wherein when one O atom and one S atom are present, the one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms

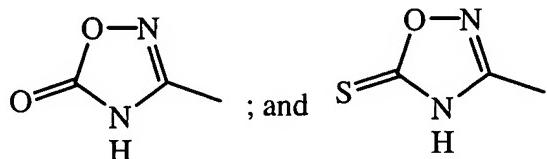
and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings; wherein a 5-membered heteroarylenyl is a 5-membered monocyclic diradical ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, wherein the 1 O atom and 1 S atom are not both present, and 6-membered heteroarylenyl is a 6-membered monocyclic diradical ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 N; wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other; wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and wherein each group and each substituent recited above is independently selected.

Claim 2 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is HO₂C.

Claim 3 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



Claim 4 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



Claim 5 (original). The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is N(R⁶)C(O).

Claim 6 (original). The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is selected from:

C≡C;
CH₂C≡C;
C≡CCH₂;
CF₂C≡C; and
C≡CCF₂.

Claim 7 (canceled).

Claim 8 (original). A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

Claim 9 (canceled).

Claim 10 (currently amended). A method for treating osteoarthritis, comprising administering to a patient suffering from osteoarthritis ~~or rheumatoid arthritis~~ a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

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Claim 11 (canceled).